A marked-up version and a clean version of claims 31-32 is attached.

REMARKS

Rejection under 35 U.S.C. § 112, first paragraph

I. **One skilled in the art will be able to practice the present invention without undue experimentation**

Enablement rejection:

On page two of Paper No. 15, the Office Action maintains the rejection of claims 25-27 and 31-33 for allegedly failing to reasonably provide enablement. The Office asserts that Claims 25-27 and 31-33 do not reasonably provide enablement for a method for determining a level or pattern of a carcinogenesis biomarker in any and/ or all cells because no evidence has been provided which teaches the correlation of patterns of carcinogenesis and increased expression of the claimed biomarkers.

Applicants disagree with this assertion and request withdrawal of this objection for the following reasons:

The test of enablement is whether one skilled in the art would be able to practice the present invention without undue experimentation. Applicants aver that the specification provides sufficient guidance to convey a reasonable expectation of success to one skilled in the art to make and use the claimed nucleic acid sequences without undue experimentation. Experimentation, even a considerable amount of experimentation, is permissible if such experimentation is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. The specification provides a means of assaying for the activity (for example, see ELISA, Western blots, HPLC-liquid chromatography, NMR, immunoprecipitations, immunoflourescence, BIA, MALDI-TOF, microarrays, PCR and hybridization assays described on pages 24-27) and have shown that the sequences have the desired activity. A utility (measuring carcinogenicity) is described in the present application and therefore the "how to use" requirement of

35 U.S.C. § 112, first paragraph, is fulfilled. The specification also describes a number of recombinant protein expression systems that have become standard in the art for the expression of proteins (page 24). One skilled in the art would be able to use the sequences and the disclosed assays without undue experimentation. Therefore, the "how to make" requirement is also fulfilled.

MPEP §2107.03 states that the applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, all that is required is a reasonable correlation between the activity and the asserted use.

Applicants submit that the present claims are enabled an request withdrawal of the 35 U.S.C. §112, first paragraph rejection.

Rejections under 35 U.S.C. § 102

I. **35 U.S.C. § 102 Rejections to claims 31-35 on basis of Hillman, Upton, and Lee were not made**

102 Rejection:

On page three of the Office Action, the Office maintained a rejection of claims 31-35 under 35 U.S.C. § 102 (e) as being anticipated by Hillman *et al.*, under 35 U.S.C. § 102 (b) as being anticipated by Upton *et al.*, under 35 U.S.C. § 102 (b) as being anticipated by Lee *et al.*, and 35 U.S.C. § 102 (b) as being anticipated by Skoda et al.

Applicants submit that no rejection of claims 31-35 under 35 U.S.C. §102 (e) on the basis of Hillman *et al.* is pending (see, for example, pages 7-8 in Paper No. 12). Applicants believe claims 31-35 stand ready for allowance.

Applicants submit that no rejection of claims 31-35 under 35 U.S.C. §102 (b) on the basis of Upton *et al.* is pending (see, for example, pages 7-8 in Paper No. 12). Applicants believe claims 31-35 stand ready for allowance.

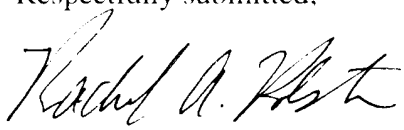
Applicants submit that no rejection of claims 31-35 under 35 U.S.C. §102 (b) on the basis of Lee *et al.* is pending (see, for example, pages 7-8 in Paper No. 12). Applicants believe claims 31-35 stand ready for allowance.

On page 8 of Paper No. 12, the Office rejected claims 31-33 as being anticipated by Skoda *et al.* Applicants have amended claims 31-32 to read on SEQ NOs: 280, 317, 384, 465, and 488. Claims 33-35 depend on claim 32. Applicants further submit that Skoda *et al.* does not disclose SEQ NOs: 280, 317, 384, 465, and 488. Because present claims 31-35 as amended do not read on subject matter disclosed in Skoda *et al.*, Applicants request that the 102 (e) rejection in light of Skoda be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe that all claims now active in the present application are in condition for allowance. Therefore, passage of the application and claims to issue is requested.

Respectfully submitted,



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:
Bunch, R. T. et al.
SERIAL NUMBER: 09/490,609
FILED: January 25, 2000
GROUP ART UNIT: 1635
EXAMINER: J. Zarra
DATE: July XX, 2002
TITLE: BIOMARKERS AND ASSAYS FOR CARCINOGENESIS

APPENDIX TO AMENDMENT

Version of Claims with Markings to Show Changes Made

31. (twice amended) A method for measuring the carcinogenicity of a composition comprising:

(A) culturing a cell line;

(B) exposing said cell line to said composition; and

(C) determining the presence or absence of mRNA which substantially hybridizes to [an] at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, 317, [337,] 384, 465, and 488 and complements thereof.

32. (twice amended) A method for measuring the carcinogenicity of a composition comprising:

(A) exposing a cell, tissue sample, or test mammal to said composition; and

(B) determining the presence or absence of mRNA in said cell, tissue sample, or test mammal which substantially hybridizes to an at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, 317, [337,] 384, 465, and 488 and complements therof.